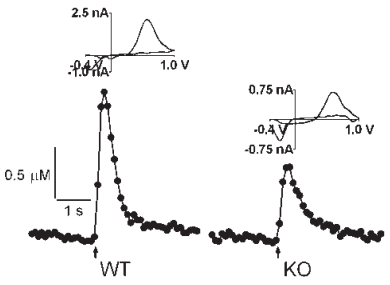
Dopamine and Fragile X Syndrome

Dopamine is an abundant neurotransmitter that plays a significant role in diverse processes such as cognition, movement, reward, memory, and learning. Now, Fulks et al. (DOI: 10.1021/cn100032f) utilize fast-scan cyclic voltammetry to measure dopamine release and uptake in mice that model fragile X syndrome, the most commonly inherited form of mental retardation.

The authors show that dopamine release is impaired in older (those 15 or 20 weeks old), while it remains unchanged in younger ones (those 10 weeks old). The drug amphetamine releases dopamine and inhibits the uptake of the neurotransmitter and was used in behavioral studies. The authors also show that 15-week-old fragile X syndrome mice are behaviorally resistant to amphetamine. This study suggests that behaviors observed in fragile X syndrome may potentially be influenced by impairments in dopamine release and uptake.

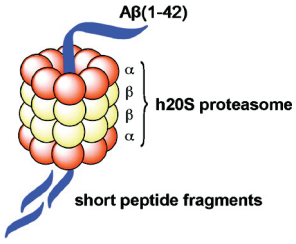


Alzheimer's Disease and Aβ Peptide Degradation

The accumulation of Aβ peptides in the brains of patients with Alzheimer's disease has been postulated to be a key hallmark in disease progression. Knowledge of how Aβ is degraded and cleared is an area of increasing interest. Zhao and Yang (DOI: 10.1021/cn100067e) demonstrate for the first time that the human 20S subunit of the proteasome efficiently degrades Aβ(1−42) peptides in solution.

The authors show that the Aβ peptides are competitive substrates for the chymotrysin-like activity of the human 20S proteasome. Gel electrophoresis, LC/MS, and TOF-MS/MS studies provided evidence for the cleavage of Aβ peptides by the proteasome.

This discovery sheds new light on the mechanism of proteasome function associated with neurodegenerative disorders such as Alzheimer's disease. Taken together, this study also highlights a central pathway potentially involved in the degradation and clearance of Aβ peptides in normal and diseased cells.



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